

In the Claims:

Please amend the claims as follows:

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1. (previously amended) A nucleic acid encoding a hybrid polypeptide comprising a signal sequence and three segments, wherein the three segments are either contiguous or are separated by a spacer amino acid or spacer peptide:

(a) the first segment having the amino acid sequence of a first portion of a naturally occurring protein of a pathogenic agent, the first segment being at least eleven amino acids in length and comprising two epitopes;

(b) the second segment having the amino acid sequence of a second portion of a naturally occurring protein of a pathogenic agent, the second segment being at least eleven amino acids in length and comprising two epitopes different from the epitopes of (a); and

(c) the third segment having the amino acid sequence of a third portion of a naturally occurring protein of a pathogenic agent, the third segment being at least eleven amino acids in length and comprising two epitopes different from the epitopes of (a) and (b),

provided that either

(i) the first, second and third portions are non-contiguous portions of the same naturally occurring protein, and the sum of all three portions constitutes less than 70% of the sequence of the naturally occurring protein; or

(ii) the first, second and third portions are portions of three different naturally occurring proteins of one or more pathogenic agents.

2. (original) The nucleic acid of claim 1, wherein at least one of the segments comprises three epitopes.

3. (original) The nucleic acid of claim 1, wherein at least one of the segments comprises four epitopes.

4. (original) The nucleic acid of claim 1, wherein at least three of the epitopes are MHC class I-binding epitopes.

5. (previously amended) The nucleic acid of claim 1, further comprising  
(d) a fourth segment which has the amino acid sequence of a fourth portion of a naturally occurring protein of a pathogenic agent, the fourth segment being at least eleven amino acids in length and comprising two epitopes different from the epitopes of (a), (b) and (c).

6. (original) The nucleic acid of claim 5, wherein the fourth segment has the amino acid sequence of a portion of a naturally occurring protein that is different from the naturally occurring protein of (a).

7. (original) The nucleic acid of claim 1, wherein at least one of the segments is less than 15 amino acids in length.

8. (original) The nucleic acid of claim 1, wherein at least one of the segments has the sequence of a portion of a human papilloma virus (HPV) protein.

9. (original) The nucleic acid of claim 1, wherein each of the naturally occurring proteins is an HPV protein.

10. (original) The nucleic acid of claim 1, wherein at least two of the segments are contiguous.

11. (original) The nucleic acid of claim 1, wherein the three segments are contiguous.

12. (original) The nucleic acid of claim 1, wherein the first and second segments are separated by a spacer amino acid or a spacer peptide and the second and third segments are separated by a spacer amino acid or a spacer peptide.

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13. (original) The nucleic acid of claim 1, wherein the first and second segments are separated by a spacer amino acid and the second and third segments are separated by a spacer amino acid.

14. (original) The nucleic acid of claim 1, wherein the first and second segments are separated by a spacer amino acid which is alanine and the second and third segments are separated by a spacer amino acid which is alanine.

15. (original) The nucleic acid of claim 12, wherein each of the naturally occurring proteins is an HPV protein.

16. (original) The nucleic acid of claim 13, wherein each of the naturally occurring proteins is an HPV protein.

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17. (original) The nucleic acid of claim 14, wherein each of the naturally occurring proteins is an HPV protein.

18. (original) The nucleic acid of claim 8, wherein the hybrid polypeptide comprises a first epitope from an HPV protein and a second epitope which does not overlap with the first epitope and which is from the same or a different HPV protein, wherein the first epitope binds to a first major histocompatibility complex (MHC) class I allotype and the second epitope binds to a second MHC class I allotype different from the first MHC class I allotype.

19. (original) The nucleic acid of claim 18, wherein at least one of the portions is from an HPV E6 or HPV E7 protein.

20. (original) The nucleic acid of claim 18, wherein at least one of the portions is from an HPV strain 16 protein or an HPV strain 18 protein.

21. (original) The nucleic acid of claim 18, wherein at least one of the portions is from an HPV E6 or E7 protein of HPV strain 16 or 18 origin.

22. (original) The nucleic acid of claim 18, wherein the first MHC class I allotype is selected from the group consisting of HLA-A1, HLA-A2, HLA-A3, HLA-A11, and HLA-A24.

23. (original) The nucleic acid of claim 22, wherein the second MHC class I allotype is selected from the group consisting of HLA-A1, HLA-A2, HLA-A3, HLA-A11, and HLA-A24.

24. (original) The nucleic acid of claim 18, wherein the hybrid polypeptide further comprises a third epitope from an HPV protein, wherein the third epitope binds to a third MHC class I allotype different from the first and second MHC class I allotypes.

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cont 25. (original) The nucleic acid of claim 18, wherein the hybrid polypeptide comprises 10 MHC class I allotype-binding epitopes from one or more HPV proteins.

26. (original) The nucleic acid of claim 18, wherein the hybrid polypeptide comprises 40 MHC class I allotype-binding epitopes from one or more HPV proteins.

27. (original) The nucleic acid of claim 18, wherein the hybrid polypeptide comprises 60 MHC class I allotype-binding epitopes from one or more HPV proteins.

28. (original) The nucleic acid of claim 24, wherein the first epitope overlaps with the third epitope.

29. (original) The nucleic acid of claim 1, wherein the signal sequence and the first segment are separated by a spacer amino acid or a spacer peptide.

30. (original) The nucleic acid of claim 1, wherein the hybrid polypeptide comprises ten MHC class I-binding epitopes from one HPV protein.

31. (original) The nucleic acid of claim 1, comprising  
(a) a first plurality of HLA-binding epitopes from an HPV strain 16 E6 protein, and  
(b) a second plurality of HLA-binding epitopes from an HPV strain 16 E7 protein;  
wherein each of the HLA-binding epitopes binds to one or more allotypes selected from the group consisting of HLA-A1, HLA-A2, HLA-A3, HLA-A11, and HLA-A24.

32. (original) The nucleic acid of claim 1, comprising  
(a) a first plurality of HLA-binding epitopes from an HPV strain 18 E6 protein, and  
(b) a second plurality of HLA-binding epitopes from an HPV strain 18 E7 protein,  
wherein each of the HLA-binding epitopes binds to one or more allotypes selected from the group consisting of HLA-A1, HLA-A2, HLA-A3, HLA-A11, and HLA-A24.

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33. (original) The nucleic acid of claim 1, comprising  
(a) a first plurality of HLA-binding epitopes from an HPV strain 16 E6 or E7 protein, and  
(b) a second plurality of HLA-binding epitopes from an HPV strain 18 E6 or E7 protein,  
wherein each of the HLA-binding epitopes binds to one or more allotypes selected from the group consisting of HLA-A1, HLA-A2, HLA-A3, HLA-A11, and HLA-A24.

34. (original) The nucleic acid of claim 1, comprising  
(a) a first plurality of HLA-binding epitopes from an HPV strain 16 E6 protein,  
(b) a second plurality of HLA-binding epitopes from an HPV strain 16 E7 protein,  
(c) a third plurality of HLA-binding epitopes from an HPV strain 18 E6 protein, and  
(b) a fourth plurality of HLA-binding epitopes from an HPV strain 18 E7 protein,  
wherein each of the HLA-binding epitopes binds to one or more allotypes selected from the group consisting of HLA-A1, HLA-A2, HLA-A3, HLA-A11, and HLA-A24.

35. (original) The nucleic acid of claim 31, wherein each plurality of epitopes comprises at least five epitopes, each of which binds to one or more of the allotypes.

36. (original) The nucleic acid of claim 31, wherein each plurality of epitopes comprises at least 15 epitopes, each of which binds to one or more of the allotypes.

37. (original) A nucleic acid encoding a hybrid polypeptide comprising a signal sequence and three segments, wherein the three segments are either contiguous or are separated by a spacer amino acid or spacer peptide:

(a) the first segment having the amino acid sequence of a first portion of a naturally occurring HPV protein, the first segment being at least eleven amino acids in length and comprising two epitopes;

(b) the second segment having the amino acid sequence of a second portion of a naturally occurring HPV protein, the second segment being at least eleven amino acids in length and comprising two epitopes different from the epitopes of (a); and

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(c) the third segment having the amino acid sequence of a third portion of a naturally occurring HPV protein, the third segment being at least eleven amino acids in length and comprising two epitopes different from the epitopes of (a) and (b),  
provided that either

(i) the first, second and third portions are non-contiguous portions of the same naturally occurring HPV protein, and the sum of all three portions constitutes less than 70% of the sequence of the naturally occurring protein; or

(ii) the first, second and third portions are portions of two or three different naturally occurring HPV proteins.

38. (original) The nucleic acid of claim 37, wherein at least one of the segments comprises three epitopes.

39. (original) The nucleic acid of claim 37, wherein at least one of the segments comprises five epitopes.

40. (original) The nucleic acid of claim 37, wherein at least three of the epitopes are MHC class I-binding epitopes.

41. (original) The nucleic acid of claim 37, further comprising  
(d) a fourth segment which has the amino acid sequence of a fourth portion of a naturally occurring HPV protein, the fourth segment being at least eleven amino acids in length and comprising two epitopes different from the epitopes of (a), (b) and (c).

42. (original) A DNA encoding a hybrid polypeptide the sequence of which comprises at least one of the following segments of HPV strain 16 E6:

AMFQDPQERPRKLPQLCTEL (SEQ ID NO:64),  
LLRREYDYDFARDLCIVYRDGNPY (SEQ ID NO:65), and  
KISEYRHYCYSLYGTTLEQQYNK (SEQ ID NO:66),

and at least one of the following segments of HPV strain 16 E7:

TLHEYMLDLQPETTDLYSY (SEQ ID NO:67),  
QAEPDRAHYNIVTF (SEQ ID NO:68), and  
LLMGTLGIVCPICSQKP (SEQ ID NO:69),

provided that the hybrid polypeptide does not comprise a sequence identical to the sequence of either full length, intact E6 or full length, intact E7 protein from HPV strain 16.

43. (original) The DNA of claim 42, wherein the hybrid polypeptide comprises at least three of the segments.

44. (original) The DNA of claim 42, wherein the hybrid polypeptide comprises all six of the segments.

45. (canceled)

46. (original) A DNA encoding a hybrid polypeptide the sequence of which comprises at least one of the following segments of HPV strain 18 E6:

RRPYKLPLDCTELNTSLQDIEITCVYCKTVLELTVFEFAFK (SEQ ID NO:152),  
and

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SVYGDTLEKLTNTGLYNLLIRCLRCQK (SEQ ID NO:153),  
and at least one of the following segments of HPV strain 18 E7:  
KATLQDIVLHLEPQNEIPV (SEQ ID NO:154),  
HTMLCMCKCEARI (SEQ ID NO:155), and  
AFQQLFLNTLSFVCPWC (SEQ ID NO:156),  
provided that the hybrid polypeptide does not comprise a sequence identical to the sequence of  
either full length, intact E6 or full length, intact E7 protein from HPV strain 18.

47. (previously amended) A DNA encoding a hybrid polypeptide the sequence of which  
comprises at least one of the following segments of HPV strain 16 E6:

AMFQDPQERPRKLPQLCTEL (SEQ ID NO:64),  
LLRREVYDFAFRDLCIVYRDGNPY (SEQ ID NO:65), and  
KISEYRHYCYSLYGTTLEQQYNK (SEQ ID NO:66);

at least one of the following segments of HPV strain 16 E7:

TLHEYMLDLQPETTDLYSY (SEQ ID NO:67),  
QAEPDRAHYNIVTF (SEQ ID NO:68), and  
LLMGTLGIVCPICSQKP (SEQ ID NO:69);

at least one of the following segments of HPV strain 18 E6:

RRPYKLPLDLCTELNTSLQDIEITCVYCKTVLELTVFEFAFK (SEQ ID NO:152),

and

SVYGDTLEKLTNTGLYNLLIRCLRCQK (SEQ ID NO:153),

and at least one of the following segments of HPV strain 18 E7:

KATLQDIVLHLEPQNEIPV (SEQ ID NO:154),  
HTMLCMCKCEARI (SEQ ID NO:155), and  
AFQQLFLNTLSFVCPWC (SEQ ID NO:156),

provided that the hybrid polypeptide does not comprise a sequence identical to the sequence of  
either full length, intact E6 or full length, intact E7 protein from HPV strain 16 or 18.

48. (original) The DNA of claim 47, wherein the hybrid polypeptide comprises at least  
five of the segments.



49. (original) The DNA of claim 47, wherein the hybrid polypeptide comprises all eleven of the segments.

50. (original) The DNA of claim 49, wherein the hybrid polypeptide further comprises a targeting signal.

51. (original) The DNA of claim 50, wherein the targeting signal comprises the HLA-DR $\alpha$  leader sequence (SEQ ID NO:63).

52. (previously amended) A DNA encoding a hybrid polypeptide the sequence of which comprises a signal sequence and at least one of the following segments of HPV E6 and E7 proteins:

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AMFQDPQERPRKLPQLCTEL (SEQ ID NO:64),  
LLRREVDFAFRDLCIVYRDGNPY (SEQ ID NO:65),  
KISEYRHYCYSLYGTTLEQQYNK (SEQ ID NO:66),  
TLHEYMLDLQPETTDLYSY (SEQ ID NO:67),  
QAEPDRAHYNIVTF (SEQ ID NO:68),  
RRPYKLPDLCTELNTSLQDIEITCVYCKTVLELTEVFEFAFK (SEQ ID NO:152),  
SVYGDTLEKLTNTGLYNLLIRCLRCQK (SEQ ID NO:153),  
KATLQDIVLHLEPQNEIPV (SEQ ID NO:154),  
HTMLCMCCCKCEARI (SEQ ID NO:155), and  
AFQQLFLNTLSFVCPWC (SEQ ID NO:156);

provided that the hybrid polypeptide does not comprise a sequence identical to the sequence of either full length, intact E6 or full length, intact E7 protein from HPV strain 16 or 18.

53. (original) A plasmid or viral vector comprising the nucleic acid of claim 1.

54. (original) The hybrid polypeptide encoded by the nucleic acid of claim 1.

55. (original) A microsphere comprising a polymeric matrix or shell and the nucleic acid of claim 1.

56. (original) The microsphere of claim 55, wherein the polymeric matrix or shell consists essentially of a polymer of poly-co-glycolic acid (PLGA).

57. (original) A therapeutic composition comprising the nucleic acid of claim 1 and a pharmaceutically acceptable carrier.

58. (original) The therapeutic composition of claim 57, further including an adjuvant.

59. (original) A liposome comprising the nucleic acid of claim 1.

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60. (currently amended) A method of eliciting an immune response in a mammal, which method comprises administering the nucleic acid of claim 1 directly to a mucosal tissue of ~~to~~ the mammal.

61. (original) The method of claim 60, wherein the mammal is a human.

62. (original) The method of claim 61, wherein the pathogenic agent is HPV and the human suffers from, or is at risk of, a condition selected from the group consisting of exophytic condyloma, flat condyloma, cervical cancer, respiratory papilloma, conjunctival papilloma, genital-tract HPV infection, cervical dysplasia, high grade squamous intraepithelial lesions, and anal HPV infection.

63. (canceled)

64. (currently amended) The method of claim 60 ~~63~~, wherein the mucosal tissue is vaginal or anal tissue.

65. (currently amended) A method of eliciting an immune response in a mammal, which method comprises administering the nucleic acid of claim 1 to the mammal ~~The method of claim 60,~~ wherein the nucleic acid is administered subcutaneously or intramuscularly.

66. (currently amended) A method of eliciting an immune response in a mammal, which method comprises administering the microsphere of claim 55 directly to a mucosal tissue of the mammal.

67. (canceled)

68. (original) The nucleic acid of claim 1, wherein the first, second and third portions are portions of one or more naturally occurring proteins of one or more viruses which infect cells.

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69. (original) The nucleic acid of claim 1, wherein the first, second and third portions are portions of one or more naturally occurring proteins of one or more pathogenic agents selected from the group consisting of HPV, human immunodeficiency virus (HIV), herpes simplex virus (HSV), hepatitis B virus (HBV), hepatitis C virus (HCV), mycobacteria, *Helicobacter spp.*, *Chlamydia spp.*, and a parasitic eukaryote which infects cells.

70. (new) The method of claim 65, wherein the mammal is a human.

71. (new) The method of claim 70, wherein the pathogenic agent is HPV and the human suffers from, or is at risk of, a condition selected from the group consisting of exophytic condyloma, flat condyloma, cervical cancer, respiratory papilloma, conjunctival papilloma, genital-tract HPV infection, cervical dysplasia, high grade squamous intraepithelial lesions, and anal HPV infection.

72. (new) The method of claim 66, wherein the mammal is a human.

73. (new) The method of claim 72, wherein the pathogenic agent is HPV and the human suffers from, or is at risk of, a condition selected from the group consisting of exophytic condyloma, flat condyloma, cervical cancer, respiratory papilloma, conjunctival papilloma, genital-tract HPV infection, cervical dysplasia, high grade squamous intraepithelial lesions, and anal HPV infection.

74. (new) The method of claim 66, wherein the mucosal tissue is vaginal or anal tissue.

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75. (new) A method of eliciting an immune response in a mammal, which method comprises administering the microsphere of claim 55 to the mammal, wherein the microsphere is administered subcutaneously or intramuscularly.

76. (new) The method of claim 75, wherein the mammal is a human.

77. (new) The method of claim 76, wherein the pathogenic agent is HPV and the human suffers from, or is at risk of, a condition selected from the group consisting of exophytic condyloma, flat condyloma, cervical cancer, respiratory papilloma, conjunctival papilloma, genital-tract HPV infection, cervical dysplasia, high grade squamous intraepithelial lesions, and anal HPV infection.

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